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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MOSHER, MARY	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/929,918	Applicant(s) KORDYUM ET AL.	
	Examiner Mary E. Mosher, Ph.D.	Art Unit 1648	

-- The MAILING DATE of this communication appears on th cover sheet with the correspond nce address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *01 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-22 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-22 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 14, line 29. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-22 and 24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 41-64 of copending Application No. 09/859,651. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims involve transforming cells with an expression plasmid, infecting the cell with lambda, and delaying lysis of the cells, to produce

soluble, biologically active proteins. The claims differ in scope, in that the each set of claims specify some elements in more detail than the other set of claims (e.g. this application's claims specify a T7 expression plasmid, the copending application's claims specify a eukaryotic gene and particular lambda mutations). However, T7 expression vectors are a well-known type of expression plasmid, and the instant claims encompass the additional details regarding expression of a eukaryotic gene and the particular lambda mutations.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-22 and 24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending allowed Application No. 09/929,945. The claims in the copending application are not currently available to the examiner; however, the claims originally filed in the application (as seen in the published application 20020155532) indicate substantially overlapping subject matter. Compare claims 1, 12-17, and 24 with original claims 1, 14, and 21 of the copending application, for example. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass the subject matter claimed in the other application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

Claims 1-22 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1-22 require "cultivating the E. coli host cell under a culture condition that induces lytic growth of said cell without lysis until a desired level of production of said protein is reached, wherein said protein is produced as a soluble, biologically-active protein." Key

elements of the invention are "induc[ing] lytic growth," "without lysis until a desired level of production of said protein is reached," and "said protein is produced as a soluble, biologically-active protein."

The intended goal, producing soluble, biologically-active protein from E. coli, is well recognized in the art as being an unpredictable matter, since recombinant proteins are frequently made in insoluble and/or inactive form. Where the invention involves an unpredictable art, the presence or absence of working examples becomes relevant to the enablement of the invention.

In reviewing the working examples, the working examples do produce soluble, biologically active protein, but none of the working examples illustrate the invention as claimed. None of the working examples have a step of cultivating the host cell under a culture condition that induces lytic growth. Each working example indicates that the protein-producer host cell was infected with phage, induced with IPTG, and cultivated at 21°C for 14 hours. After the 14 hours, the cultures were centrifuged, and the supernatant was harvested. There is no step of inducing lytic growth in the protein-producing cells. In the working examples, an induction step appears to be involved only in preparing the phage to be used in infection. Therefore, the method used in the working examples differs materially from the method recited in the claims.

Furthermore, the specification does not teach how to determine whether or not " a desired level of production of said protein is reached" in cells during cultivation, or how to control the timing of lysis until after that point. The specification teaches that one can control the timing of induction with the cI857 mutation, but once induction has occurred, the specification does not teach how to controllably delay lysis "until a desired level of production" of protein is reached.

Considering the unpredictability of the art (obtaining soluble, biologically active protein), the incomplete teachings in the specification (preventing lysis until a desired level of production is reached), and the absence of working examples (inducing lytic growth in the transformed,

infected host cell), it is concluded that undue experimentation would be required to practice the invention as claimed in claims 1-22.

In claim 24, the claim requires infecting a transformed cell with a temperature-sensitive lambda phage, incubating the infected cells "such that protein is produced and released into the culture medium upon lysis... as a soluble, biologically-active protein at a concentration greater than 100 microgram/ml." Again, the invention involve the unpredictable art of producing soluble, biologically active protein. Again, although the working examples produce soluble, biologically active protein, but the working examples do not teach lysis of the producer cells. The working examples further do not teach the concentration of the protein in the culture medium. Considering the unpredictability of the art, the limited teachings of the specification, and the absence of working examples, it is concluded that undue experimentation would be required to practice the invention as claimed.

Conclusion

Claims 1-22 and 24 are seen as free of the art. In the prior art, Chen et al (Journal of Biotechnology 40:87097, 1995) and Lin et at (Biotechnology and Bioengineering 57:529-35, 1998) disclose delayed lysis mutants of bacteriophage lambda, used for increasing the production of recombinant protein expressed from a lambda vector by extending the period where genes are expressed from the replicating lambda vector. These references do not provide any motivation to combine delayed lambda lysis with a plasmid expression vector. Auerbach et al (US 4637980) and Breeze (GB 2143238) teach induction of a lambda lysogen for lysing cells expressing a protein product. Auerbach teaches one embodiment with delayed lysis because of lower expression of lysozyme from the lambda prophage (bacterial host strain UC5822), and teaches that this embodiment produces a superior yield of recombinant protein, see Example 9. However, neither Breeze nor Auerbach provides motivation to transform the cell with a plasmid first, then infect the cell with the lambda phage. Breeze and Auerbach begin with a cell containing a

lysogenic prophage; Auerbach then introduces an expression plasmid. There does not appear to be a logical reason to reverse the order of steps, since reversing the order requires additional work to prepare the phage for infecting the transformed cells, and one is not assured of infecting every transformed cell. In the method taught by Breeze and Auerbach, every transformed cell already contains the phage, so every protein-producing cell in the culture will be induced and lysed. The prior art also fails to teach or suggest delaying lysis using lambda mutants in N, Q, or R genes (claim 6), or delaying lysis by using a high multiplicity of infection (claim 11).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone numbers for this Group are now (703) 872-9306 for Before Final responses, and (703) 872-9307 for After Final responses. Faxes for this Group can also be sent to (708) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

9/12/03

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600